

REMARKS

Attached hereto is a marked-up version of the changes made to the specification, sequence listing and claims by the current amendment. The attached marked-up version is captioned "**Version with markings to show changes made.**"

Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at line 8, page 1 has been amended as follows:

[This application is a continuation-in-part of "ENERGY TRANSFER DYES WITH ENHANCED FLUORESCENCE," Application Serial No.: 08/642,330; Filed: May 3, 1996 and U.S. Application Serial No.: 08/672,196; filed June 27, 1996; entitled: "4,7-DICHLORORHODAMINE DYES" which are incorporated herein by reference.]

This application is a continuation of U.S. Application Serial No. 09/272,097, filed on March 18, 1999, which is a continuation of U.S. Application Serial No. 09/046,203, filed on March 23, 1998, now Patent No. 5,945,526, which is a continuation of U.S. Application No. 08/726,462, filed on October 4, 1996, now Patent No. 5,800,996, which is a continuation-in-part of U.S. Application No. 08/672,196, filed on June 27, 1996, now U.S. Patent No. 5,847,162 which is a continuation-in-part of U.S. Application No. 08/642,330, filed on May 3, 1996, now Patent No. 5,863,727, each of which it is incorporated herein by reference in its entirety.

The paragraph beginning at line 20, on page 10, has been amended as follows:

In another embodiment, the energy transfer fluorescent dyes have donor and acceptor dyes with the general structure where Y_1 and Y_2 taken separately are either hydroxyl, oxygen, iminium or amine, the iminium and amine preferably being a tertiary iminium or amine and $[R_{11}-R_{17}]$ $R_{11}-R_{16}$ are any substituents which are compatible with the energy transfer dyes of the present invention.

Page 52 has been amended as follows:

In compound [3a] 3A-A, one of R_1 and R_2 is ethyl, the other being hydrogen, R_3 and R_4 taken separately are hydrogen, $[R_5]$ R_6 is methyl, $[R_6-R_{10}]$ R_5 and R_7-R_{10} taken separately

are hydrogen, X_1 is carboxylate, and one of X_3 and X_4 is a linking group, the other being hydrogen.

In compound [3b] 3A-B, one of R_1 and R_2 is ethyl, the other being hydrogen, R_3 and R_4 taken separately are methyl, R_5 is methyl, R_6 - R_{10} taken separately are hydrogen, X_1 is carboxylate, and, one of X_3 and X_4 is a linking group, the other being hydrogen.

In compound [3c] 3A-C, R_1 and R_2 taken separately are methyl, R_3 and $[R_7] R_9$ taken together form a six membered ring, R_4 and R_8 taken together form a six membered ring, R_5 , R_6 , $[R_9] R_2$, and R_{10} taken separately are hydrogen, X_1 is carboxylate, and, one of X_3 and X_4 is a linking group, the other being hydrogen.

In compound [3d] 3B-D, R_1 and R_2 taken separately are hydrogen, R_3 and $[R_7] R_9$ taken together form a six membered ring, R_4 and R_8 taken together form a six membered ring, R_5 , R_6 , $[R_9] R_2$, and R_{10} taken separately are hydrogen, X_1 is carboxylate, and one of X_3 and X_4 is a linking group, the other being hydrogen.

In compound [3e] 3B-E, one of R_1 and R_2 is ethyl, the other being hydrogen, R_3 and $[R_7] R_9$ taken together form a six membered ring, R_4 and R_8 taken together form a six membered ring, R_5 is methyl, R_6 , $[R_9] R_2$ and R_{10} taken separately are hydrogen, X_1 is carboxylate, and, one of X_3 and X_4 is a linking group, the other being hydrogen.

In compound [3f] 3B-F, R_1 and R_2 taken separately are hydrogen, R_3 and R_4 taken separately are methyl, R_5 - R_{10} taken separately are hydrogen, X_1 is carboxylate, and, one of X_3 and X_4 is linking group, the other being hydrogen.

The paragraph beginning at line 5, on page 53 has been amended as follows:

Figure 4A shows a generalized synthesis wherein the substituent X_1 can be other than carboxylate. In the figure, X' indicates moieties which are precursors to X_1 . In the method illustrated in Figure 4A, two equivalents of a 3-aminophenol derivative [4a/4b] 4A-A/4A-B, such as 3-dimethylaminophenol, is reacted with one equivalent of a dichlorobenzene derivative [4c] 4A-C, e.g., 4-carboxy-3,6,dichloro-2-sulfobenzoic acid cyclic anhydride, i.e., where the X_1' moieties of 4c taken together are,

The paragraphs beginning at line 14, on page 53, have been amended as follows:

The reactants are then heated for 12 h in a strong acid, e.g., polyphosphoric acid or sulfuric acid, at 180°C. The crude dye [4d] 4A-D is precipitated by addition to water and isolated by centrifugation. To form a symmetrical product, the substituents of reactants [4a] 4A-A and 4b are the same, while to form an asymmetrical product, the substituents are different.

Figure 4B shows a generalized synthesis wherein the substituent X₁ is carboxylate. In the method of Figure 4B, two equivalents of a 3-aminophenol derivative [4a/4b] 4A-A/4A-B, such as 3-dimethylaminophenol, is reacted with one equivalent of a phthalic anhydride derivative [4e] 4B-E, e.g. 3,6-dichlorotrimellitic acid anhydride. The reactants are then heated for 12 h in a strong acid, e.g., polyphosphoric acid or sulfuric acid, at 180°C. The crude dye [4d] 4A-D is precipitated by addition to water and isolated by centrifugation. To form a symmetrical product, the substituents of reactants [4a] 4A-A and [4b] 4A-B are the same, while to form an asymmetrical product, the substituents are different.

The paragraph beginning at line 23, page 93, has been amended as follows:

Dye primer sequencing was performed on the [M13 (SEQ. ID. NO.: 2)] pGEM (SEQ. ID. NO.: 3) using a set of four dyes attached to the M13-21 primer (SEQ. ID. [NO. 3] NO.: 2) as described in Example 5. Figure 13 is a four color plot of the dye labeled oligonucleotides produced from the sequencing. The peak for cytosine corresponds to the fluorescence of 5-CFB-DR110-2. The peak for adenosine corresponds to the fluorescence of 6-CFB-DR6g-2. The peak for guanosine corresponds to the fluorescence of 5-CFB-DTMR-2. The peak for thymidine corresponds to the fluorescence of 5-CFB-DROX-2.